Physiology’s Impact: Exploring the Mysteries of Life

The discipline of physiology explores the mysteries of life. How is it possible that the same organism can live in a dangerous environment, where extreme ambient temperatures, gravitational forces, oxygen availability, or other abiotic factors impose serious challenges to the maintenance of homeostasis? Clearly, our continued survival depends on our bodies being adaptive. We can explore these physiological adaptations through experiments of nature where evolution has shaped various strategies to meet environmental demands. Comparative physiologists have the world as their laboratories and the diversity of life as their experimental models. The fascination with life in all its forms relates to our striving for wellness and health. We are all subject to stress, whether self-imposed or in response to our environment. Environmental physiologists are at the forefront of this search for physiological understanding of our response to stress. In Physiology, we publish review articles that explore a wide range of themes. In this issue, we comment on two of these themes: responding to our environment and striving for wellness.

Responding to Our Environment: Learning Through Comparative Physiology

“I want to say a word for the study of comparative physiology also for its own sake. You will find in the lower animals mechanisms and adaptations of exquisite beauty and the most surprising character, and I think nothing can be more fascinating than the senses and instincts of insects as revealed by modern investigations.” With these words, the Danish Nobel laureate Professor August Krogh ended his important opinion papers in the American Journal of Physiology, where he also defined the August Krogh principle: “for such a large number of problems there will be some animal of choice, or a few such animals, on which it can be most conveniently studied” (6). This fascination with animals persists today, and comparative studies that address how animals survive hostile environments and exhibit extreme behaviors appeals to the curiosity of any person. It is not surprising, therefore, that many popular nature programs on television or articles in newspapers and popular journals use the impressive achievements of animals, such as cheetahs that sprint at speeds exceeding 100 km/h, snakes that can eat more than their own body mass, or geese that fly in extreme hypoxia when crossing the Himalayas, to engage their audience.

Because the enormous diversity of animals also represents a true plethora of physiological and anatomical structures, comparative physiology often provides excellent examples to understand how general principles apply to all animals. The respiratory system is an excellent example in this context, where aquatic vertebrates rely on gills for gas exchange in water, whereas air-breathing vertebrates use lungs. Insects represent a rather different solution, where the tracheal system—an elaborate air-filled set of tubes that penetrate the individual organs—conveys O₂ uptake and CO₂ excretion. Nevertheless, as explained by Harrison et al. (5), gas exchange through this system is governed by the same laws of diffusion and convection as the mammalian lung, despite the enormous anatomical differences.

In addition to appealing to our immediate inquisitiveness of understanding how these animals function, it often turns out that animals living under extreme conditions provide excellent avenues to understand a given scientific problem (i.e., the August Krogh principle). For example, in the current issue of Physiology, Panneton (10) reviews the classic diving response, where heart rate decreases and systemic vascular resistance increases during submersion. Panneton shows how the neural circuits responsible for these physiological responses are similar among all mammals (in fact they are probably very similar among all air-breathing vertebrates), but that the diving response is much more pronounced in aquatic species and represents an important contribution to the long breath-holds of diving mammals. Similarly, fish that survive in extremely high salinities have not invented completely novel physiological mechanisms to secure water and salt balance but have modified existing ion transport systems to conquer hostile environments (7). Thus it is becoming increasingly clear that the evolutionary adaptations that allow animals to thrive in extreme environments often merely require modifications of existing physiological mechanisms or biochemical pathways.

A remarkable example of how common functional problems often result in similar evolutionary solutions is exemplified through the comparison of echolocation in bats and whales in the current issue (9). Although bats spend most of their time flying in the air, whereas whales are deeply submerged in water for most of their lives, they face very similar problems, namely that vision does not suffice in either the dark nights or the black abyss. Through an independent and hence convergent evolution, both bats and whales have evolved biosonar systems through which these animals actively produce sound and use the returning echoes to navigate and locate prey in very similar ways.

Our rather recent ability to understand the physiological adaptations that allow whales to hold their breath and manage O₂ stores during prolonged diving and the understanding of the exquisite biosonar systems in the wild is really only possible because of recent major advances in techniques that allow us to record complex animal behaviors in their natural environment to address their physiology. Thus, as the sensors that can monitor physiological variables or movements can be made smaller and smaller, and the electronic storing devices are also miniaturized and made less energy consuming, we can now employ measuring devices on or within animals and track their movement patterns while also performing measurements of heart rate, sound production, etc. Although this research area is merely in its infancy, it is already clear that the behavioral repertoire of wild animals vastly exceeds what we know from laboratory studies.
**Striving for Wellness: Relationship Between Stress and Wellness**

How is it that stress, in all of its forms, can be both healthy and unhealthy for humans? Certainly impact depends not only on the type of stress but also on whether the stress is acute or chronic. If we think of stress as purely physiological, such as occurs with exercise, our responses to stress are orchestrated to help us adjust physiologically to maintain allostatic and keep us alive. Acutely, our bodies are designed for exercise to help us escape a threatening environment, to chase down a meal, or to get from place to place. Following repeated acute exercise stresses (i.e., exercise training), the body goes through an incredible degree of adaptation and change to allow us to exercise longer, faster, and more efficiently. Friedrich Nietzsche described this concept as “That which does not kill us, makes us stronger.” It has now become clear that, as we have adapted to more sedentary lives, repeated bouts of acute exercise stress are more effective than medication at mitigating the risks of cardiovascular disease. That exercise may be the best medicine is the focus of an article submitted to this issue of Physiology (4).

The classic concept of “stress” and our ability to adapt to it was championed by Walter Cannon in the early part of the last century in his book Bodily Changes in Pain, Hunger, Fear, and Rage (2). His “flight or fight” response described the changes in physiological regulation by the sympathetic nervous system. Some of these responses include increasing blood pressure, redistributing blood flow, raising heart rate and contractility, and activating the adrenal glands to release epinephrine and cortisol. In the context of acute exercise, these physiological changes allow us to better adjust and respond to the imposed challenge. With repeated exercise stress, resulting adaptations protect our cardiovascular system and ultimately make us healthier (8).

But when stress is a bad thing, it is important to understand how and why it impacts our well being. The same physiological responses that allow us to benefit from exercise can also cause us to become sick when they are chronically activated. In the case of repeated acute exercise stress (as opposed to chronic stress), the individual bouts of acute stress are interspersed by periods of rest and adaptation, as described by Hans Selye’s General Adaptation Syndrome. In the case of psychological stress, there may be no “rest” period to allow for recovery from the acute activation of the sympathetic nervous system. We now understand that, when the sympathetic nervous system is chronically activated, there are a number of maladaptations that occur, leading to dysfunction and increased risk for disease (3). As the definition of health has evolved from merely the presence or absence of disease to a broader spectrum between wellness and illness, chronic stress not only increases the risk and severity of disease but additionally reduces our ability to adapt to positive stressors and maintain optimal health and wellness. As one example, chronic sympathetic nervous system activation can reduce β-adrenergic receptor sensitivity, which is quite concerning, considering the important role these receptors play in exercise-mediated vascular adaptations and cardioprotection (1). Since women rely on greater β-adrenergic receptor-mediated vasodilation than men to buffer changes in sympathetic outflow, they may be at even greater risk for hypertension resulting from chronic sympathetic overdrive (11) and may not achieve the same beneficial vascular adaptations to exercise.

On a more personal note, we ask the question, “How well do we translate all we have learned from studying stress physiology to our own work and lives?” In our very biased view, all physiologists need to consider the acute and chronic effects of various stressors on the pathway, process, or disease state they are interested in studying. In addition, keeping the consequences of chronic stress in mind is important on other fronts. Being a student or scientist is not a stress-free endeavor, and our laboratories are not typically stress-free environments. There are many pressures placed on us, including (but certainly not limited to) trying to get grants funded in a very challenging and competitive environment and convincing reviewers and editors to accept our work, because in our view it’s the most important ever and our careers depend on getting manuscripts in top journals. Many of us do not manage stress well, and despite our knowledge of the physiological risks of chronic stress, we do not do enough to care for ourselves. Hopefully the manuscripts published in Physiology on “Striving for Wellness” will serve as a reminder to engage in self-care. Regular exercise, of course, is excellent for managing chronic stress. But there are many other options, including yoga, tai-chi, mediation, or dancing. The point is that stress physiology is fun and important to study, and has direct application both to our research and to managing our own health and well being. As leaders in the discovery of the benefits and risks associated with various types of stress, we have an obligation to serve as role models to our families and communities by applying what we learn in the laboratory to our daily lives. In fact, our lives depend on it!

**References**